

**WHAT IS CLAIMED IS:**

1. A method for generating an established cell line which produces hepatitis C virus (HCV) comprising transforming peripheral blood mononuclear cells (PBMCs) which produce HCV with Epstein Barr virus (EBV).  
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2. The method of claim 1, wherein said cells producing HCV, are in a peripheral blood lymphocyte (PBL) fraction of said PBMCs.
3. The method of claim 2, wherein said cells producing HCV, are B-cells.
- 10 4. The method of any one of claims 1 to 3, wherein said HCV produced by said established cell line enables the replication of complete and infectious HCV.
- 15 5. A method for producing HCV *in vitro* comprising:
  - a) generating an established cell line which produces hepatitis C virus (HCV) comprising transforming a B-cell which produces HCV, with Epstein Barr virus (EBV);
  - b) growing the EBV-immortalized B-cell obtained in a) in culture under conditions enabling HCV production.
- 20 6. The method of claim 5, wherein conditions in b) comprise a stimulation of said EBV-immortalized B-cell to produce HCV.
7. The method of claim 5 or 6, wherein said B-cell is present in a PBMC or PBL.

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8. The method of claim 7, wherein said PBMC or PBL fraction is obtained from a HCV positive patient which is immunosuppressed.

9. The method of claim 8, wherein said  
5 immunosuppression is due to injection drug use of said patient.

10. The method of claim 7, wherein said PBMC or PBL fraction is obtained from a HCV positive patient which has not been treated with interleukin.

11. The method of any one of claims 5 to 10, further  
10 comprising a co-cultivation of said EBV-immortalized B-cell, which is stimulated to produce HCV in the presence of monocyte-derived dendritic cells (DCs).

12. The method of any one of claims 6 to 11, wherein  
15 said stimulating is carried out using an HCV replication activating-inducing amount of at least one mitogen.

13. An EBV-established B-cell line capable of replicating complete and infectious HCV.

14. A cell-based *in vitro* replication system for HCV  
20 comprising an EBV-transformed B-cell capable of replicating complete and infectious HCV, and a second cell population having HCV tropism and in which robust HCV replication occurs, so that under appropriate culture conditions said second cell population can become infected by said infectious HCV produced by said EBV-transformed B-cell.

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15. The cell-based replication system of claim 14, further comprising appropriate culture media reagents conditions enabling infection of said second cell population.

16. The cell-based replication system of claim 14 or 15, wherein said second cell population is peripheral blood lymphocytes (PBLs).

17. The cell-based replication system of claim 14, 15 or 16, wherein said second cell population is a cell line.

18. An assay for screening a test agent and selecting an agent which possesses anti-HCV activity, comprising:

- a) growing a EBV-immortalized cell line which produces HCV, or culturing said EBV-immortalized cell line with a second cell population so as produce HCV from said second cell population; and
- b) assaying a biological function of said HCV produced from said cell line or said cell population.

19. The assay of claim 18, wherein said biological function is selected from the group consisting of binding to a cellular receptor of HCV, replication, translation, assembly, and infectivity.

20. A method for identifying, from a library of compounds, a compound with anti-HCV activity, comprising:

- a) providing a screening assay according to claim 18 or 19;
- b) contacting said screening assay with at least one compound from said library; and

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c) detecting if said at least one compound inhibits a biological activity of HCV;  
wherein a test compound which inhibits said biological activity is a compound with said anti-HCV activity.

- 5                    21. The method of claim 20, wherein the test compound with said anti-HCV activity is further modified by combinatorial or medicinal chemistry to provide further analogs of said test compound also having said therapeutic effect.